

## REMARKS

In response to the Office Action of October 29, 2004, Applicants respectfully request the Examiner to reconsider the rejection of claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55 as well as claims 8-10, 24, 37-41, 43-45, 47-50, 56 and 57 dependent thereon, under both the written description and enablement provisions of 35 U.S.C. §112, first paragraph, based on the remarks hereinbelow. In addition, Applicants have added new claims 60-92 which further define subject matter to which Applicants are entitled. Favorable consideration of all pending and newly submitted claims is respectfully requested.

New independent claims 60-62, 66-69, 71-74 recite methods employing, and transgenic plants comprising, in relevant part: “a nucleic acid molecule encoding a plant cyclin-dependent kinase inhibitor (CKI) which binds a plant cyclin-dependent kinase having a PSTAIRE cyclin-binding motif, wherein the nucleic acid molecule encoding the plant CKI is under the control of a promoter which functions in a plant cell, and wherein the CKI comprises the amino acid sequences set forth in SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36, or wherein the CKI comprises the amino acid sequences set forth in SEQ ID NO: 34, SEQ ID NO:35, and SEQ ID NO:36, wherein one or more of the sequences set forth in SEQ ID NO: 34, SEQ ID NO:35, and SEQ ID NO:36 has one amino acid substitution therein”. This language is similar to language previously recited in claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55, i.e., the language “or any of the aforementioned amino acid sequences having one mismatch at any position.” The previously-recited language was deleted by the amendment filed May 25, 2004, in order to advance prosecution of the present application with respect to a new-matter rejection.

Upon further consideration by Applicants, new claims 60-92 have been added in order to further define the subject matter to which Applicants are entitled.

Support for the subject matter recited in new claims 60-92 may be found throughout the specification, e.g., page 53, line 5, to page 55, line 18 (which includes paragraphs (b) through (f) on page 55). Table 2 of the application provides basis for amino acid substitutions other than those covered by the strict limitations of SEQ ID NO: 34 to SEQ ID NO: 39. Thus, the motifs having the amino acid sequences set forth in SEQ ID NOs: 34-39 do not, in some instances, cover the motifs as they appear in the various CKIs (ICKs, KRPs)(see Table 2) unless one amino acid substitution is taken into account. For example, the CKIs discussed below would not fall within the scope of the consensus sequences SEQ ID NOs. 34, 35, or 36 unless one amino acid substitution is taken into account.

With respect to the consensus sequence SEQ ID NO: 34 (FX<sub>2</sub>KYNFD), Applicants respectfully submit the following. *Arabidopsis* CKI2 (also known as FL39 or ICK2 or KRP2) and having the amino acid sequence as set forth in SEQ ID:2, contains one amino acid substitution within this consensus sequence (see Table 2 for ICK2: motif 1 in which the first amino acid residue is indicated as a C in contrast to an F set forth in SEQ ID NO:34). Therefore, claims which recite SEQ ID NO:34, without accounting for one amino acid substitution, would not even cover the ICK2 exemplified by the present application (see Example 16) since SEQ ID NO: 34 indicates the first amino acid to be an phenylalanine (F).

With respect to the consensus amino acid sequence set forth in SEQ ID NO: 35 (P/LLXGRYEW), *Arabidopsis* ICK2 (CKI2, FL39) contains 1 amino acid substitution

within this consensus sequence (*see* Table 2 for ICK2 motif 2 in which the second amino acid is indicated as a G, whereas according to the sequence represented by SEQ ID NO: 35, the amino acid indicated at this position is an L). Therefore, without accounting for one substitution, CKI2 would not be covered by the claims when directed towards this particular consensus sequence. Similarly, *see* Table 2 for ICK4: motif 2 in which the sixth amino acid is indicated as an F, whereas according to the sequence represented by SEQ ID NO: 35, the amino acid residue indicated at this position is a Y). Therefore, without accounting for one amino acid substitution, ICK4 would not be covered by the claims when directed towards this particular consensus sequence. See also Table 2 for the *Chenopodium* ICK2: motif 2 in which the penultimate amino acid is indicated as a D, whereas the sequence represented by SEQ ID NO: 35 indicates an E at this position. Therefore, without accounting for one amino acid substitution, this ICK would also not be covered by the claims when directed towards this particular consensus sequence.

With respect to SEQ ID NO: 36 (EXED/EFFX<sub>3</sub>E), *Arabidopsis* ICK4 (=FL67, *see* Figure 1 of the present application) and the alfalfa ICK sequence provided by the present application (see Example 14 and SEQ ID NO:6), each contain one amino acid substitution within this consensus sequence. See Table 2 for ICK4: motif 3, in which the third amino acid is indicated as a D. Therefore, without taking into account one amino acid substitution, CKI4 would not be covered by the claims when directed towards this particular consensus sequence. *See also* Table 2 for the alfalfa sequence motif 3, in which the sixth amino acid is indicated as a C, which is not the amino acid residue indicated in SEQ ID NO: 36 for this position. Therefore, without taking into account one

substitution, the alfalfa CKI (ICK) would not be covered by the claims when directed towards this particular consensus sequence.

It is respectfully submitted by Applicants that as taught by the present application, in some instances, a CKI will have the consensus sequences as set forth in SEQ ID NOs: 34-36. *See e.g.*, ICK5 in Table 2. As also taught by the present application however, in some instances a CKI will have the consensus sequences as set forth in SEQ ID NOs: 34-36 taking into account one amino acid substitution as summarized in the preceding three paragraphs. Because plant CKIs often do not exhibit “perfect” consensus sequences corresponding to SEQ ID NOs: 34-36, the present application teaches, e.g., at page 54 last paragraph to page 55, paragraph (f), that plant CKIs may be characterized as having the consensus sequences SEQ ID NOs: 34-39 or else “a peptide that is at least 70% identical thereto.”

It is respectfully submitted that the language “wherein one or more of the sequences set forth in SEQ ID NO:34, SEQ ID NO:35, and SEQ ID NO:36 has one amino acid substitution therein” presently recited in new claims 60-62, 66-69, and 71-74 does not constitute the addition of new matter to the specification as originally filed. Nor does the recitation in claims 89 and 90 of “wherein the CKI further comprises the consensus amino acid sequence as set forth in any one of SEQ ID NO:37, SEQ ID NO:38, or SEQ ID NO:39 having one amino acid substitution” constitute the addition of new matter to the application as originally filed. Although the above-quoted language might not be found *ipsis verba* in the specification, as described above, the specification clearly teaches such limitation.

Applicants respectfully submit that the proper test for sufficiency of description in a patent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time, of the later claimed subject matter.” *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983).

Exactly how the specification allows one skilled in the art to recognize that an applicant had possession of the claimed invention is not material. *In re Smith*, 481 F.2d 910, 178 USPQ 279 (CCPA 1973). Typically, an applicant conveys that he or she is in possession of the invention by use of descriptive means such as “words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 UAPQ2d 1961, 1966 (Fed. Cir. 1997). To comply with the written description requirement, it is not necessary that the application describe the invention *ipsis verbis*. *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971). What is required is that an ordinarily skilled artisan recognize from the disclosure that applicants invented the subject matter of the claims, including the limitations recited therein. *Smith*, 481 F.2d at 915, 178 USPQ at 284.

Thus, it has been well settled that the written description requirement of 35 U.S.C. § 112, first paragraph, can be satisfied without express or explicit disclosure of a later-claimed invention. *See e.g. In re Herschler*, 591 F.2d 693, 700, 200 USPQ 711, 717 (CCPA). In that particular case, the court stated: “[t]he claimed subject matter need not be described in *haec verba* to satisfy the description requirement. It is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants

invented processes including those limitations.” (citations omitted). *See also Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000)(“In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *en haec verba* support for the claimed subject matter at issue.”).

It is respectfully submitted that the consensus sequences set forth in SEQ ID NOs:34-39 having one amino acid substitution, although not recited *en haec verba* in the specification, are nevertheless described clearly in the specification, so that one skilled in the art would recognize that Applicants invented the presently claimed methods and compositions including the limitations recited therein. In view of the remarks hereinabove, favorable consideration of new claims 60-92 is warranted.

Turning to the Office Action of October 29, 2004, claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55, as well as claims 8-10, 24, 37-41, 43-45, 47-50, 56 and 57 dependent thereon, remain rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. It is the Examiner’s position that “[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.” *See* October 29, 2004 Office Action, page 2, final paragraph to page 3.

The first reason for maintaining the rejection is set forth on page 4 of the office action, where the Examiner posits that “[t]he rejection is maintained, however, because plant CKIs that comprise amino acid sequences at least 70% identical to disclosed

conserved amino acid motifs (SEQ ID NOS:34-39) are not adequately described, literal support for the recitation of at least 70% identical thereto notwithstanding.”

The Examiner readily admits that the specification provides literal support for the recitation of plant CKIs comprising amino acid sequences at least 70% identical.

The Examiner’s position is apparently that “[w]hile some of the disclosed plant CKI amino acid sequences which are the basis for the conserved amino acid motifs of SEQ ID NOS:34-39 exhibit some variation (1-2 specific amino acids) in these motifs, they only exhibit variation at specific positions in each motif.” Office Action, page 4.

What the Examiner is asserting therefore, is that despite the fact that the specification provides literal support for the recitation in the claims of plant CKIs comprising amino acid sequences at least 70% identical to the sequences set forth SEQ ID NOS:34-39, and despite the fact that the specification provides examples of plant CKIs comprising the plant CKI consensus sequences discovered by the present invention, which sequences are at least 70% identical to the sequences set forth SEQ ID NOS:34-39 which function in the methods and compositions of the present invention, the written description requirement is allegedly not met by the present claims.

The Examiner’s assertion at page 4, lines 15-18 that “[n]either the specification nor the prior art describe plant CKIs that comprise 2 to 3 unspecified amino acids at any unspecified position in each motif” is unclear. Both the specification and prior art certainly disclose different CKIs having at least 70% sequence identity to the disclosed sequence motifs SEQ ID NOS: 34-39. In many of these exemplified CKIs, one amino acid residue is substituted in the sequences set forth in SEQ ID NOS: 34-39. It is the present invention that discovered the sequence motifs set forth in SEQ ID NOS: 34-39 as

well as the fact that different CKIs may vary with respect to the sequence identity to the consensus sequences set forth in SEQ ID Nos:34-39.

The Examiner's statement at page 5, last line, to page 6, line 2, that "one skilled in the art would not know on the basis of the disclosure which of the 20 different amino acid residues would occupy which of the eight of ten available positions in each of the recited motifs that plant CKIs comprise" is not relevant in a proper written description determination since predictability is not the legal standard or test for rejections under the written description requirement. *See Ex parte Yuejin Sun, 2003 Pat. App. LEXIS 65* (Bd. Pat. Appl. & Inter., February 27, 2003), provided herewith as Exhibit A. Moreover, the Examiner's characterization in the last line of page 5 to page 6, line 1, of what a skilled artisan faces having the present application in hand is inaccurate. Such an artisan would not be faced with not knowing "which of the 20 different amino acids would occupy which of the eight to ten available positions in each of the recited motifs." Rather, a skilled artisan having in hand the consensus sequences provided by the present application and set forth in SEQ ID NO:34-39 as well as other teachings provided by the present application, would have known that other plant ICKs may be identified and used in the methods and compositions of the present invention by using the consensus sequences provided by SEQ ID NOS:34-39 as a guide and that such identified other plant ICKs might certainly have sequences at least 70% identical to any of SEQ ID NOS:34-39.

At pages 6 to 10 of the Office Action, the Examiner lists different CKIs, disclosed by the present application, which have specific amino acid substitutions compared to the consensus sequences set forth in SEQ ID NOS: 34-39. These pages of the Office Action, appear to be the predicate for the Examiner's position that Applicants are only entitled to



methods and compositions comprising CKIs having these specific substitutions. On the contrary, however, these pages of the Office Action only serve to advance Applicants' position: that the present application more than adequately described a representative number of species presently embraced by the claims. Moreover, as the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112 ¶1, "Written Description" Requirement, *Fed. Reg.* Vol. 66, No. 4, Friday, January 5, 2001, make clear on page 1106: "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces."

For the record, Applicants respond to the Examiner's characterization of plant CKIs having the consensus sequences provided by the present invention. For example, the statement on page 4 of the Office Action that "SEQ ID NO:35 may specifically vary at one of two positions", is incorrect. Plant ICKs are known to vary at 4 positions in the consensus sequence SEQ ID NO:35. See Table 2 which clearly shows that the 8 amino acid sequence motif may vary at position 2 (e.g., in ICK2), position 6 (e.g., ICK4), position 7 (e.g., ICK6, ICK7, and *Chenopodium* ICK), and in position 8 (e.g., Alfalfa ICK). The Examiner has stated on page 4 of the Office Action that "SEQ ID NO:36 may specifically vary at one of two positions". Table 2 of the application clearly indicates, however, that plants vary in three different positions in SEQ ID NO:36. For example, alfalfa ICK varies at position 6, ICK4 and ICK7 both vary at position 3, and ICK6 varies at position 5.

Applicants also correct the record as follows. Page 7, lines 3-5 of the Office Action should indicate that for SEQ ID NO:35, *six* (not four) of the disclosed plant CKIs

have a consensus sequence that varies from the consensus sequence of SEQ ID NO:35, and each varies by one amino acid at *four* (not two) different locations. The Examiner apparently did not consider alfalfa ICK and ICK2.

Page 7, lines 15-16 should indicate that for SEQ ID NO:36, *four* (not three) of the nine disclosed plant CKIs have a consensus sequence that varies from the consensus sequence of SEQ ID NO:36 and each varies by one amino acid substitution at *three* (not two) different locations. Applicants direct the Examiner to ICK6, which was apparently not considered by the Examiner. On that same page, last two lines to page 7, line 2, *four* (not three) of the nine disclosed plant CKIs have a consensus sequence that is less than 100% identical to the consensus sequence set forth in SEQ ID NO:36. Again, the Examiner apparently did not consider ICK6.

Finally, with respect to page 10, lines 5-9, the Examiner states: “[w]ith respect to the rice plant CKI ICK2, the Examiner maintains that the rice plant CKI ICK2 cannot support the description of the plant CKIs recited in the claims because the rice plant CKI ICK2 was identified after the present application was filed, and the written description requirement must be met at the time of filing”, Applicants respectfully submit the following. The showing made in the rule 132 declaration submitted previously, that rice plant CKI ICK2 was identified following the teachings of the present invention, albeit after the present application was first filed, is appropriate since it demonstrates how one skilled in the art relied on the teachings of the present application as originally filed. Thus, while it is true that a later dated disclosure cannot supplement an insufficient disclosure in a prior dated application, the use of later publications (in this case, the later disclosure of rice CKI ICK2 submitted as part of the Rule 132 declaration) as evidence of

the state of the art existing on the filing date of the application is appropriate. *See e.g. In re Hogan* 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977). As submitted by Dr. Wim Van Camp in paragraphs 13-15 of the Rule 132 declaration submitted May 25, 2004, one of skill in the art in identifying rice CKI ICK2 and using this CKI in practicing the presently claimed invention, relied upon the written description of the present application. *See* declaration under 37 C.F.R. § 1.132, paragraph 14: “[c]onsensus sequences having at least 70% identity to the amino acid sequences set forth in SEQ ID NOs: 34, 35, and 36 and present in the corresponding rice amino acid sequences were used to identify the rice cDNA as encoding an ICK.”

Further in this regard, submitted herewith is a declaration under 37 C.F.R. §1.132 executed by Dr. Catherine Bergounioux, Research Director of the Cell Cycle Laboratory, Institute of Plant Biotechnology, CNRS, France. As stated in paragraph 5 of the declaration, Dr. Bergounioux is co-author of an article published in the *Journal of Cell Science* 115(5), 973-982, 2002. This paper, provided at Exhibit B of the declaration, is entitled “The CDK inhibitor NtKIS1 is involved in plant development, endoreduplication and restores normal development of cyclin D3; 1-overexpressing plants.” As discussed in paragraph 6 of the declaration submitted herewith, the published article describes a CKI from tobacco, NtKIS1a, and the phenotypic characteristics of *Arabidopsis* plants transformed with the corresponding *NtKIS1a* gene under the control of the constitutive cauliflower mosaic virus 35S promoter. The transformed 35S::NtKIS1a plants showed reduced growth with smaller organs that contained larger cells; reduced CDK kinase activity, serrated leaves and reduced endoreduplication. These phenotypic characteristics are the same as those described in the above-identified application and as described in a

publication by De Veylder *et al.*, The Plant Cell, Vol 13, 1653-1667, July 2001 (provided as Exhibit C to the declaration).

As stated in paragraph 7 of the declaration, although Dr. Bergounioux and her co-authors used NtKIS1a in the paper provided at Exhibit B, it is Dr. Bergounioux's scientific belief that other CKI proteins could also be used to achieve the same results. Her basis for this statement is her finding that the tobacco CKI, NtKIS1a, comprises a first sequence motif which is identical to the sequence set forth in the above-identified application as SEQ ID NO:34 as well as a second sequence motif comparable but not identical to the consensus sequence set forth in the above-identified application as SEQ ID NO:35 and a third sequence motif comparable but not identical to the consensus sequence set forth in the above-identified application as SEQ ID NO:36. Specifically, in NtKIS1a (NCBI Accession Number CAC82732), the sequence comparable to SEQ ID NO: 35 is: PSEGRYEW and the sequence comparable to SEQ ID NO: 36 is: EIEDFFAVRQ. The differences in the motifs of the tobacco sequences compared to the consensus sequences set forth in Table 2 (SEQ ID NOs: 35 and 36) of the above-identified application are underlined and boldfaced.

The consensus sequences of SEQ ID NO: 34, SEQ ID NO: 35 and SEQ ID NO: 36 (and also of consensus sequences SEQ ID NO: 37, SEQ ID NO: 38 and SEQ ID NO: 39) were also described in Table 1 of De Veylder *et al.* (see Exhibit C of the declaration). Table 1 of De Veylder *et al.* is identical to Table 2 of the above-identified application except that Motif 1 of Table 1 is equivalent to Motif 2 or SEQ ID NO: 35 of Table 2 of the present application; and Motif 5 of Table 1 is equivalent to Motif 6 or SEQ ID NO: 39 of Table 2 of the present application. As taught on page 53 of the above-identified

application, as well as column 1, page 1655 of the De Veylder publication provided at Exhibit C of the Bergounioux declaration, the three domains located at the extremity of the C-terminal part of the proteins are shared by all CKIs (= KRPs) and are therefore important in identifying plant CKIs. It is Dr. Bergounioux's considered scientific opinion therefore, that one skilled in the art following the teachings of the above-identified application as of its filing date, as well as the literature extant at the time of filing, would have known that NtKIS1a was a CKI due to the presence of these three consensus sequences (SEQ ID NOs:34-36). These three consensus sequences were first provided in the written description of the present application.

Finally, the Examiner maintains on page 10 of the Office Action that an assertion that Applicants were in possession of plant CKIs that comprise amino acid sequences at least 70% identical to the disclosed conserved amino acid motifs of SEQ ID NOS: 34-39 does not substitute for a description of same because as set forth by *Enzo Biochem v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1617, a showing of possession alone does not satisfy the written description requirement.

In response to this position of the Examiner, Applicants respectfully submit that Applicants have repeatedly demonstrated much more than a conclusion that they were in possession of the presently claimed invention as of the filing date. Rather, Applicants have provided a written description of the genus of plant CKIs "sufficient to distinguish it from other materials." See e.g., *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1567, 43, USPQ2d 1398, 1405 (Fed. Cir. 1997). The Examiner has been directed to specific amino acid sequences specifically described in the present application and the prior art, as well as to specific teachings in the present application for using such

sequences in the methods and compositions of the present invention. Applicants have further repeatedly demonstrated during prosecution of this application, that CKIs which bind a plant cyclin-dependent kinase having a PSTAIRE cyclin-binding motif, wherein the CKIs comprise the amino acid sequences as set forth in SEQ ID NOs:34, 35, and 36 or else comprise amino acid sequences having at least 70% identities to the amino acid sequences as set forth in SEQ ID NOs:34, 35, and 36, or alternatively, amino acid sequences corresponding to SEQ ID NOs: 34-36 having one amino acid substitution therein, may be used for decreasing or increasing cyclin dependent kinase activity in a plant, thereby obtaining plants with various phenotypes as presently claimed.

It is respectfully submitted, that the Examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the consensus sequences set forth in SEQ ID NOs:34-39 as well as sequences at least 70% identical to SEQ ID NOs:34-39, would be unable to recognize, upon reading the present application, that Applicants invented the claimed subject matter. Dr. Bergounioux in her declaration under 37 C.F.R. §1.132, submitted herewith, *has* however, set forth facts upon which she has predicated her recognition from the disclosure of the present application, that Lieven DeVeylder et al., the applicants of the present application, invented the subject matter of the claims, including the limitations recited therein. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55, as well as claims 8-10, 24, 37-41, 43-45, 47-50, 56 and 57 dependent thereon, under the written description requirement of 35 U.S.C. §112, first paragraph.

Claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55, as well as claims 8-10, 24, 37-41, 43-45, 47-50, 56 and 57 dependent thereon, have also been rejected under the

enablement requirement of 35 U.S.C. §112, first paragraph. The position of the Examiner is that the specification allegedly does not reasonably provide enablement for methods of using a nucleotide sequence encoding a plant cyclin-dependent kinase inhibitor which binds a plant cyclin-dependent kinase having a PSTAIRE cyclin-binding motif wherein the CKI comprises an amino acid sequence that is at least 70% identical to SEQ ID NO:34, SEQ ID NO:35 and SEQ ID NO:36. The Examiner also alleges on page 11 of the Office Action that the specification also does not reasonably provide enablement for methods of using a nucleotide sequence encoding a plant cyclin-dependent kinase inhibitor which binds a plant cyclin-dependent kinase having a PSTAIRE cyclin-binding motif wherein the CKI comprises an amino acid sequence that is at least 70% identical to “SEQ IDNO:37 or SEQ ID NO:37 or SEQ ID NO:38”, (*sic*, SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39.) According to the Examiner, “the full scope of the invention is not enabled because the functional effects of altering an amino acid sequence is unpredictable, since the functionality of an amino acid consensus sequence may depend on the presence of particular amino acids at particular positions in the consensus sequence.” Office Action, page 11, last paragraph.

On page 12 of the Office Action, the Examiner cites Faustinella F., et. al., (May 25, 1991) *J. Biol. Chem.* 266(15):9481-5, for the teaching that some amino acid substitutions involving each of eight serine residues of human lipoprotein lipase inactivate its enzymatic activity and some do not. Applicants submit that the relevance of human lipoprotein lipase to plant CKIs is unclear. In any event, the authors were able to make the amino acid substitutions and readily test for enzyme activity using well known methodologies.

Ogata S. et al. (1992) Biochemistry 31(9): 2582-5, has been cited by the Examiner for teaching that different types of amino acid substitutions in a consensus sequences in dipetidyl peptidase IV have different effects on enzyme activity. Again, the relevance of this protein, found in the brush border of small intestine and kidney proximal tubules, to plant CKIs is unclear. Importantly, the authors were able to readily perform site-directed mutagenesis followed by transfection/expression experiments, using well known procedures in order to ascertain which substitutions had positive effects and which substitutions had negative effects on enzyme activity.

Zhu, J., et al. (Sept. 1993) Proc. Natl. Acad. Sci. 90(18):8557-61, has been cited for its teaching that different types of amino acid substitutions in a consensus sequence that functions in protein isoprenylation have different effects. Although the protein comprising the consensus sequence, ANJ1 is a plant protein (unlike the other proteins cited by the Examiner), its relevance to plant CKIs is unclear. In this particular protein, substitution of S for C in the CAQQ motif of ANJ1 eliminated isoprenylation of ANJ1, whereas substitution of the amino acid L for the terminal amino acid Q did not result in loss of enzyme activity. Again, the authors were able to readily perform site-directed mutagenesis followed by transfection/expression experiments, using well known procedures in order to ascertain which substitutions had positive effects and which substitutions had negative effects on enzyme activity.

In contrast to these three examples, the present application provides in Table 2, *ten different plant ICKs*, each comprising the different consensus sequences SEQ ID NO: 34, 45, and 36, and in many instances, having an amino acid substitution in these consensus sequences. With respect to the consensus sequences set forth in SEQ ID NO:



37, two out of the six CKIs listed have an amino acid substitution. With respect to SEQ ID NO: 39, two out of four of the CKIs listed in Table 2 have amino acid substitutions. ICK5, in particular, has two amino acid substitutions within the consensus sequence. All of the nine different plant CKIs listed in Table 2 have been shown to work in the methods and compositions of the presently claimed invention.

The present application provides guidance to a skilled artisan as to how to locate and use a plant CKI in the methods and compositions of the present invention. At the time the present application was filed, a number of CKIs from different plant species were publicly available for use in the methods and compositions of the present invention. These CKIs are listed in Table 2 and either have perfect identity to the presently disclosed consensus sequences or else exhibit greater than 70% sequence identity thereto. Since the filing date of the present application, even more CKIs have become available, each exhibiting the consensus sequences provided by the present invention, including consensus sequences exhibiting at least 70% amino acid sequence identity thereto.

The consensus sequences provided by the present invention help in the identification of the CKI. As stated on page 54 of the present application, "overall homology between plant ICKs is very low, i.e., lower than 40% whereas identities are under 30%. This hampers the identification of novel ICK genes in plants. Therefore, the delineation of conserved motifs is of utmost importance to enhance identification of said novel plant ICK genes." Page 53 of the present application provides that the consensus sequences provided in Table 2, are comprised in the carboxy-terminal part of plant ICK proteins and are conserved in all plant ICKs known to date.

Aside from structure, the present application also provides functional information for helping identify a plant CKI which binds a plant cyclin-dependent kinase having a PSTAIRE binding motif as presently recited by the claims. Thus, for example, examples 1-2 outline a two hybrid screening assay useful to identify a CDC2aAt-interacting protein, i.e., a protein binding to a protein having a PSTAIRE binding motif. Example 4 provides an *in vivo* assay for ascertaining binding exclusivity to a protein having a PSTAIRE binding motif. An assay for ascertaining inhibition of kinase activity, the functional activity of a plant CKI, is provided by Example 6 of the present application. An *in vitro* assay for ascertaining binding exclusivity to a protein having a PSTAIRE binding motif is provided by Example 7.

Applicants respectfully submit that the Examiner has not established that the combination of the disclosures of the chemical structures of the amino acid sequences set forth in SEQ ID NOs: 2, 4, and 6, corresponding to different plant CKIs, as well as the nucleotide sequences encoding same, i.e., SEQ ID NOs: 1, 3, and 5, teachings in the specification of how to test for CKI activity, general overall sequence identities of plant CKIs and those specific consensus sequences set forth in SEQ ID NOs: 34, 35, 36, 37, 38, and 39, including peptides having a least 70% identity thereto which would encompass the specific amino acid substitutions set forth in Table 2, would be insufficient to identify a plant protein as a plant CKI. The Examiner has also not established that one of ordinary skill in the art having the above-described chemical structure teaching in hand as well as the ability to test for PSTAIRE protein binding exclusivity, and inhibition of kinase activity as taught by the present application (outlined above) would be unable to identify a plant protein as being a plant CKI. Nor has the

Examiner established that once a plant CKI was identified according to the assays and the consensus sequences provided by the present application, including sequences having at least 70% identity thereto, that such an identified CKI would not be reasonably expected to produce the phenotypic effects recited by the claims.

As stated by Dr. Bergounioux in the Rule 132 declaration submitted herewith, one skilled in the art can readily discern that the consensus sequences shown in Table 2 of the present application vary somewhat from plant species to plant species. It is her scientific opinion however, that one skilled in the art such as herself recognize that even if the consensus sequences vary somewhat from plant to plant, a motif in a plant having about 70% identity (or one amino acid substitution) to the consensus sequences set forth in Table 2 (SEQ ID NOs:34-39), would be reasonably expected to function in the claimed invention with predictable results. Her research group is yet another group to demonstrate such predictable results based on the teachings of the present application as detailed in her publication provided at Exhibit B of her Rule 132 declaration.

In paragraphs 6 and 7 of Dr. Bergounioux's declaration, she avers that although her group used a tobacco CKI, NtKIS1a, it is her scientific belief that other CKI proteins could also be used to achieve the same results her group achieved and the present application teaches, i.e., reduced growth, smaller organs, larger cells, reduced CDK activity, serrated leaves, and reduced endoreduplication. In paragraphs 7 and 8, Dr. Bergounioux avers that despite the fact that two out of the three consensus sequences identified in NtKIS1a comprise one amino acid substitution when compared to the consensus sequences SEQ ID NOs: 35 and 36, one skilled in the art following the teachings provided by the present application as of its filing date, as well as the literature

extant at the time of filing, would have known that NtKIS1a was a CKI due to the presence of the three consensus sequences (SEQ ID NOs: 34-36). In paragraph 9 of the declaration, Dr. Bergounioux attests to the fact that the consensus sequences shown in Table 2 of the present application vary somewhat among plant species. Her considered scientific opinion however, is that one skilled in the art would recognize that even though the consensus sequences vary among plants somewhat, a motif in a plant having about 70% sequence identity (or one amino acid substitution) to the consensus sequences set forth in Table 2 (SEQ ID NOs: 34-39), would be reasonably expected to function in the claimed invention with predictable results. The publication provided at Exhibit B of the declaration clearly demonstrates Dr. Bergounioux's own personal knowledge of the facts upon which her opinion is based, i.e., transformed 35S::NtKIS1a plants.

In summary, by her Rule 132 declaration, Dr. Bergounioux has provided facts sufficient on which to base her opinion that if she had had in hand both the disclosure of the present application as well as the literature extant on the filing date of the present application, she would have had every reasonable expectation of success in practicing the presently claimed invention. *See* paragraph 10 of the Rule 132 declaration submitted herewith. In addition, as averred in paragraph 10 of the declaration submitted herewith, without having to engage in undue experimentation, one skilled in the art such as Dr. Bergounioux would have had every reasonable expectation of success in practicing the presently claimed invention using a plant CKI comprising the consensus sequences set forth in SEQ ID NOs:34-36 and/or SEQ ID NOs: 34-37 and/or SEQ ID NOs:34-39, including sequences having at least 70% identity thereto (or one amino acid substitution therein).

The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (Bd Pat. App. 1982).

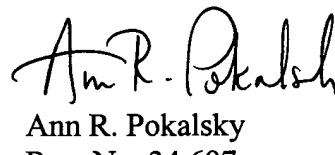
Based on the specific teachings summarized above, Applicants respectfully submit that at the time the application was first filed, upon reading the present application and the literature extant, those of ordinary skill in the art would have been provided a reasonable amount of guidance to obtain and use a plant CKI having the consensus sequences set forth in SEQ ID NOs: 34-39, including sequences having at least a 70% identity thereto. Further, a reasonable amount of guidance for using such CKIs in the methods and transgenic plants of the presently claimed invention would have also been provided. In view of the teachings and examples set forth in the specification, the previously submitted post-filing date publications which follow the teachings of the present application and confirm such teachings, the previously submitted declarations under 37 C.F.R. §1.132 as well as the declaration under 37 C.F.R. §1.132 submitted herewith, there is no evidence or sufficient reason of record why one of ordinary skill in the art would not have had a reasonable expectation of success in practicing the present invention using a CKI comprising the consensus sequences set forth in SEQ ID NOs:34-39, including sequences having at least 70% identity thereto. Accordingly, the rejection of claims 2, 5, 7, 11, 14, 17, 21, 25, 27, 30, 36, 54 and 55, as well as claims 8-10, 24, 37-

41, 43-45, 47-50, 56 and 57 dependent thereon, under the enablement provision of 35 U.S.C. §112, first paragraph, should be withdrawn.

Claims 2, 5, 7-11, 14, 21, 24-25, 27, 30, 36-41, 43-45, 47-50 and 52-57 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 4-9 and 13-23 of copending application Serial No. 10/688,291. Applicants respectfully submit that upon allowance of the claims under consideration in this application, an appropriate action will be taken in order to obviate the provisional double patenting rejection.

In view of the amendments to the claims, the submission of new claims 60-92, the declaration under 37 C.F.R. §1.132 submitted herewith, and the foregoing remarks, the present application is believed to be in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

  
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